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EXAMINER	
COOK, LISA V	
ART UNIT	PAPER NUMBER
1641	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/586,285	CHEN, FENGLIN	
	Examiner	Art Unit	
	LISA V. COOK	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7 and 13-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7 and 13-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

1. Applicant's response to the Office Action mailed 5/21/08 is acknowledged (paper filed 8/21/08). Currently claims 1, 7, and 13-15 are pending and under consideration.

2. Rejections and/or objections of record not reiterated herein have been withdrawn.

NEW GROUNDS OF REJECTIONS NECESSITATED BY AMENDMENT

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1, 7, and 13-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 1 and 15 are vague and indefinite because the claims are directed to methods that appear to read on process steps that are not clearly identified with respect to ***diagnosing and/or monitoring*** spontaneous abortion in a patient. Specifically, the claims recite that an isolated human chromosome No.2 is used as an antigen. However, this language does not positively recite that the isolated human chromosome No.2 is contacted with the patient sample, thus allowing for the formation of a complex which is measured/detected and correlated to the claimed method of diagnosing and/or predicting spontaneous abortion. Therefore, it is unclear what method/process applicant intends to cover in the claimed methods.

A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. It is suggested that an actual contact step, a step of complex formation and detection, and a correlation step relative to spontaneous abortion be added to the claims to eliminate ambiguity. Appropriate correct is required.

B. The term "suitable" in claim 14 is a relative term, which renders the claim indefinite. The term "suitable" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear as to what Applicant will consider suitable for the claimed kit. It is suggested that the term “suitable" be eliminated from the claim language. Please correct.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 7, and 15 along with dependent claims 13-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims 1, 7, and 15 were amended on 8/21/08 to recite the use of an isolated human chromosome No.2 as antigen. However support for the amendment could not be found in the originally filed specification or claims. In particular, the specification and previous claims required the use of a chromosome No. 2 containing fibronectin encoding gene. There is no support for any additional chromosome No. 2 or chromosome No.2 without fibronectin. Accordingly, this is new matter. Applicant is invited support for the claims for consideration.

5. Claims 1 and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant specification appears to suggest a link between an isolated chromosome No.2 containing fibronectin encoding gene derived from a plurality of males. See specification page 12-second paragraph and page 15-3rd paragraph for example. However, the specification does not give any information with respect to the correlation of any other chromosome No.2 (without fibronectin). The instant claims are drawn to the measurement of chromosome No.2 in recurrent spontaneous abortions (RSA). This is not taught nor supported by the disclosure or the prior art.

For example, the prior art teaches that chromosome No.2 may be linked to systemic lupus erythematosus but there is no evidence of a link to chromosome No.2 to RSA. For example, see Perdriger et al. (Joint Bone Spine, Vol.70, 2003, pages 103-108).

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation.

Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The nature of the invention- the invention is directed to a method for diagnosing and/or monitoring spontaneous abortion via an isolated chromosome No.2 antigen (without fibronectin).

The state of the prior art- the prior art of record teaches that chromosome No.2 is correlated to systemic lupus erythematosus but there is no evidence of a link to chromosome No.2. For example, see Perdriger et al. (Joint Bone Spine, Vol.70, 2003, pages 103-108).

The predictability or lack thereof in the art- there is no predictability based on the instant specification that the claimed methods will correlate an isolated chromosome No.2 (without fibronectin) to spontaneous abortion.

The amount of direction or guidance present- appropriate guidance is not provided by the specification for the claimed method to diagnose and/or monitor RSA with an isolated chromosome No.2 (without fibronectin).

The presence or absence of working examples- working examples are not provided in the specification that a show RSA with an isolated chromosome No.2 (without fibronectin).

The quantity of experimentation necessary- it would require undue amount of experimentation for the skilled artisan to make and use the methods as claimed.

The relative skill of those in the art-the level of skill in the art is high.

The breadth of the claims- as recited the instant claims are directed to a methods that is applicable to any and all responses to any and all chromosome No.2 and RSA.

While it is not necessary to show working examples for every possible embodiment, there should be sufficient teachings in the specification that would suggest to the skilled artisan that the breadth of the claimed method is enabled. This is not the case in the instant specification.

Therefore, one of ordinary skill in the art could not make and use the invention as claimed without undue experimentation.

6. Claims 1, 7, and 13-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to methods of monitoring and/or diagnosing RSA with an isolated chromosome No.2 (without fibronectin). However, the disclosure does not teach chromosome No. 2 absent fibronectin and the prior art teaches that isolated chromosome No.2 is correlated to systemic lupus erythematosus but there is no evidence of a link to RSA. For example, see Perdriger et al. (Joint Bone Spine, Vol.70, 2003, pages 103-108).

The instant specification does not exemplify a correlation between chromosome No. 2 absent fibronectin and RSA. Accordingly it is deemed that Applicant did not possess the claimed invention.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115). The skilled artisan cannot envision the detailed method of diagnosing and/or monitoring RSA by using chromosome No. 2 absent fibronectin .Thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Therefore, the full breadth of the claimed invention does not meet the written description provision of 35 USC 112, first paragraph.

Please note: the art rejections are applied with respect to the kit compositions and not the kits intended utility.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

I. Claims 7 and 14 are rejected under 35 U.S.C. 103(a) as being obvious over Bernasconi et al. (American Journal of Human Genetics, 1996, Vol.59, No.5 pages 1114-1118) in view of Foster et al. (U.S. Patent #4,444,879).

Bernasconi et al. teach the evaluation of spontaneous abortion in a 36 year old normal healthy female. The patient had five spontaneous abortions during the first three months of pregnancy.

Cytogenic investigation disclosed a female karyotype with isochomosomes of 2p and 2q replacing two normal chromosomes 2. It appeared that chromosome No.2 was important in the patient's pregnancies.

Bernasconi et al. (American Journal of Human Genetics, 1996, Vol.59, No.5 pages 1114-1118) differ from the instant invention in not specifically including isolated chromosome No.2 in kit embodiments.

However, kits are well known embodiments for assay reagents. Foster et al. (U.S. Patent #4,444,879) describe one example. In their patent kits including the reactant reagents, a microplate, positive controls, negative controls, standards, and instructions are taught. The kits include labeled antibodies (claim 14). See column 15 lines 22-23. The reagents are compartmentalized or packaged separately for utility. See figure 6, and column 15, lines 10-34.

It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to take the Chromosome No.2 reagent of Bernasconi et al. (American Journal of Human Genetics, 1996, Vol.59, No.5 pages 1114-1118) and format it into a kit because Foster et al. taught that it is convenient to do so and one can enhance sensitivity of a method by providing reagents as a kit.

Further, the reagents in a kit are available in pre-measured amounts, which eliminate the variability that can occur when performing the assay. Kits are also economically beneficial in reagent distribution.

II. Claim 13 is rejected under 35 U.S.C. 103(a) as being obvious over Bernasconi et al. (American Journal of Human Genetics, 1996, Vol.59, No.5 pages 1114-1118) in view of Foster et al. (U.S. Patent #4,444,879) and further in view of Maggio (Immunoenzyme technique I, CRC press © 1980, pages 186-187).

Please see Bernasconi et al. (American Journal of Human Genetics, 1996, Vol.59, No.5 pages 1114-1118) in view of Foster et al. (U.S. Patent #4,444,879) as set forth above.

Bernasconi et al. (American Journal of Human Genetics, 1996, Vol.59, No.5 pages 1114-1118) in view of Foster et al. (U.S. Patent #4,444,879) differ from the instant invention in not specifically teaching antigen immobilization (bound to solid support or carrier).

However, Maggio disclose enzyme immunoassays wherein either the antigen or antibody is immobilized onto a solid phase. The solid phase can be particles, cellulose, polyacrylamide, agarose, discs, tubes, beads, or micro plates (micro titer plates). See page 186. The reagents can be bound to the solid support by covalent linkage or passive adsorption (non-covalent means). See page 187 1st paragraph. Maggio taught that solid supports such as test strips “are very convenient to wash thereby reducing labor in assay procedures”. Page 186, last line.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to immobilize antibodies on solid support surfaces as taught by Maggio in the kits having utility in the assay methods including Chromosome No.2 as exemplified by Bernasconi et al. (American Journal of Human Genetics, 1996, Vol.59, No.5 pages 1114-1118) in view of Foster et al. (U.S. Patent #4,444,879) because Maggio taught that reagent immobilized solid support "are very convenient to wash thereby reducing labor in assay procedures". See page 186. Absent evidence to the contrary the immobilization of reagents is deemed and obvious modification taught by the prior art.

Response to Arguments

Applicant's arguments and amendments have been carefully considered but were not found persuasive for the following reasons:

A. Applicants amendment introducing an isolated chromosome No.2 antigen (without fibronectin) into the claims was deemed new matter and not enabled.

B. Applicants have argued that the reference to Bernasconi et al. does not teach the use of isolated human chromosome No.2 as an antigen for the diagnosis/monitoring of RSA. However, the use of a product or method of utilizing a product is not given weight in product claims (kits).

C. In response to applicant's argument that Bernasconi et al. does not teach isolated human chromosome No.2 in RSA, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use then it meets the claim.

D. Applicant contends that the use of karyotyping with chromosomes of 2p and 2q does not teach or suggest the determination of antinuclear antibodies against an isolated chromosome No.2. This argument was carefully considered but not found persuasive because an obviousness rejection is proper so long as the prior art suggests a reason or provides motivation to make the claimed invention, even where the reason or motivation is different from that discovered by applicant. *In re Dillon*, 919 F.2d 688, 696, 16 USPQ 2d 1897, 1904, (Fed. Cir. 1990) (in banc), cert.denied, 111 S.Ct. 1682, (1991).

Also, the test for obviousness is not whether the features of one reference may be bodily incorporated into the other to produce the claimed subject matter but simply what the combination of references makes obvious to one of ordinary skill in the pertinent art. See, *In re Bent*, 52 CCPA 850, 144 USPQ 28, 1964*; In re Nievelt*, 179 USPQ 224 CCPA 1973.

8. For reasons aforementioned, no claims are allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Remarks

10. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Jones (Acta Endocrinologica, 1975, Vol.78, No.Suppl94, pages 376-404, Abstract Only) disclose semen correlation to infertility.

B. Aoki et al. (American Journal of Reproductive Immunology, 1993, Vol29, pages 82-87) teach methods measuring antinuclear antibodies (ANA) as a predictive measure in recurrent abortion. The patients were treated and ANA measurements were compared to control. See entire reference.

11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya, can be reached on (571) 272-0806.

Any inquiry of a general nature or relating to the status of this application should be directed to Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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1/21/09

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Primary Examiner, Art Unit 1641